REMARKS/ARGUMENTS

Reconsideration of this application and entry of the foregoing amendments are respectfully requested.

Claims 1-41 have been cancelled without prejudice and new claims 42-61 have been added in lieu thereof. That new claims have been presented should not be construed as an indication that Applicants agree with any view expressed by the Examiner. Rather, the new claims are offered merely to advance prosecution and Applicants reserve the right to pursue any deleted subject matter in a continuation or divisional application.

The specification has been amended to include sequence identifiers and the Sequence Listing submitted herewith. The sequence presented in the new Sequence Listing corresponds to that presented on pages 7 and 34. It has been noted that the originally filed Sequence Listing and that submitted July 29, 2002 included an alanine at position 26 not present in the sequences at pages 7 and 34. Entry of the Sequence Listing submitted herewith does not raise the issue of new matter as the sequence information contained therein is presented in the application as originally filed. The computer readable copy of the Sequence Listing submitted herewith is the same as the attached paper copy of that Listing.

Claims 1, 2, 6, 7, 9 and 17 stand rejected under 35 USC 112, second paragraph, as allegedly being indefinite. Withdrawal of the rejection is submitted to be in order in view of the above-noted claim revisions and further in view of the comments that follow.

New claim 42 reads "... particles which are targeted to a targeted cell type to be detected", thereby addressing the Examiner's concerns as regards claim 1.

New claim 46 reads "a particle" rather than "the particle" thereby obviating the rejection of claim 2.

New claim 50 makes clear the first and second binding moieties thereby addressing the Examiner's concerns regarding claim 6.

New claim 51 includes a comma after "KALA" and before "and LAGA" thereby obviating the rejection of claim 7.

New claim 53 includes commas after the words "Polymixin B", "Valinomycin", and before "and Vibriolsin" thereby addressing the rejection of claim 9.

New claim 61 includes the word "a" rather "the" thereby addressing the Examiner's rejection of claim 7 based on lack of antecedent basis.

Reconsideration and withdrawal of the rejection is submitted to be in order.

Claims 1, 10, 11, 14 and 17 stand rejected under 35 USC 102(e) as allegedly being anticipated by Meers et al (USP 6,087,325). Withdrawal of the rejection is submitted to be in order for the reasons that follow.

At the outset, the Examiner's attention is redirected to the overview of the instant invention provided in the response filed October 24, 2003. Those comments are incorporated herein by reference.

Claim 1 has been revised as new claim 42 and reads "....*said particles having at least one layer of enveloping lipids and incorporating a cytolytic peptide, which peptide,*

in response to a predetermined metabolic signal from the targeted cell, if present in the sample, interacts with the layer to act as or mediate the opening of pores or channels within the lipid layer to thereby modulate the permeability of the particles...". Basis for this revision is found on page 5 (paragraphs 2 and 4), and page 6 (paragraph 2).

Applicants submit that claim 42 is novel over Meers *et al.* (US 6,087,325).

Meers et al does not disclose a particle having a peptide, which "in response to a predetermined metabolic signal from the targeted cell, interacts with the layer to act as or mediate the opening of pores or channels within the lipid layer to thereby modulate the permeability of the particles", as required by claim 42.

Meers et al describes a liposome composed of phosphatidylethanolamine (PE), which is known to be intrinsically unstable, but which is stabilized by a covalent conjugation with a peptide to the hydrophilic head group of PE. Once the peptide is cleaved by a peptidase, the peptide is simply detached from the PE, wherein the liposome falls apart, thereby releasing it's contents. Hence, there is no interaction between the peptide and the lipid layer following cleavage by the peptidase, i.e. the metabolic signal. Applicants submit that the peptide is passive, because there is no interaction with the lipid layer to modulate the permeability of the membrane, in response to the peptidase. The peptide acts merely as a 'blocking group', which, upon removal by peptidases, allows an unstable liposome to fall apart and assume it's thermodynamically stable form. Furthermore, Applicants submit that the peptide employed by Meers et al is not cytolytic,

because the liposome cannot release its contents in response to stimuli other than a peptidase.

In contrast, the particles in the present invention comprise a peptide that is actively cytolytic because it interacts with the layer of enveloping lipids to modulate the permeability of the membrane. For example, the peptide can be an ion channel, which "opens" in response to H^+, or Cl^- ions. The particles are able to release their contents in response to stimuli other than a peptidase, because the cytolytic peptide interacts with the lipid layer in response to a range of metabolic signals.

While no further comment is believed necessary, the following additional remarks are offered regarding certain of the newly presented dependent claims.

In new claim 43, the cytolytic peptide comprises an integral protein of the lipid layer. Basis for this claim is found at page 6 (paragraph 2). Claim 43 is novel over Meers et al, which discloses a peptide that is covalently bonded to the PE, such that it projects above the surface thereof (column 5, line 45 – 48). Hence, the Meers et al peptide is not integral with the lipid layer. That the protein is integral with the lipid layer enables it to interact with the layer to act as or mediate the permeability of the particle.

In new claim 44, the cytolytic peptide spans the lipid layer. Basis for this claim is found at page 6 (paragraph 2). Claim 44 is novel over Meers et al, because, as indicated above, the covalently bonded peptide projects above the surface of the carrier. Hence, the Meers et al peptide does not span the lipid layer. As with new claim 43, that the peptide

spans the lipid layer enables it to interact with the layer to act as or mediate the permeability of the particle.

In new claim 45, the cytolytic peptide is non-covalently attached to an outer lipid layer. Basis for this claim is found at page 6 (paragraph 2). Claim 45 is novel over Meers et al, which describes covalently attaching the peptide to PE to form the conjugate, as illustrated in the Figure shown on lines 13-20 of column 2.

In view of the novelty of new claim 42, the remaining claims, which depend from claim 42, are also novel.

Reconsideration is requested.

Beginning on page 6 of the Action, the Examiner sets forth a series of rejections of one or more claims as obvious under 35 USC 103 over Meers et al (USP 6,339,069) in combination with another reference. The cited Meers et al patent ('069) is a continuation-in-part of an application that issued as USP 6,143,716, which was a division of the application that issued as USP 6,087,325 (the patent upon which the Examiner rejects claims 1, 10, 14 and 17 under 35 USC 102(e)). In view of the fact that the Examiner has based the obviousness rejections on the '069 patent, rather than the '716 or '325 patent, Applicants assumes that the Examiner finds the subject matter relevant to the rejection only in the '069 patent.[1]

[1]If this assumption is in error the Examiner is requested to indicate where in the parent/grandparent cases basis for the rejection is found.

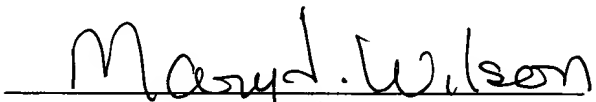
The '069 patent derives from an application filed June 29, 1999. This is after the filing date of the PCT application from which the instant case derives. Accordingly, subject matter new to the '069 patent is not citable against the instant case and any rejections based thereon must fail.[2]

In view of the above, the Examiner is urged to reconsider the rejections under 35 USC 103 and withdraw same or explain where basis is found in a document that qualifies as prior art.

This application is submitted to be in condition for allowance and a Notice to that effect is requested.

Respectfully submitted,

NIXON & VANDERHYE P.C.

By: 
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[2] Indeed, the application that issued as the '716 patent was filed October 7, 1998 and thus after the filing date of the UK application from which the instant case claims priority.